

September 10, 2007

Dear Doctor:

We are writing to inform you about key safety information regarding the use of *FENTORA*[®] (fentanyl buccal tablet) [C-II]. We have recently learned of serious adverse events, including deaths in patients treated with *FENTORA*. **These deaths occurred as a result of improper patient selection (e.g., use in opioid non-tolerant patients), improper dosing, and/or improper product substitution.** The following information is meant to emphasize key points about appropriate patient selection and proper dosing and administration of *FENTORA* to reduce the risk of respiratory depression.

Key Safety Information regarding *FENTORA*:

- **Do NOT use *FENTORA* in opioid non-tolerant patients**
- **Use *FENTORA* only for labeled indications**
- **Do not prescribe *FENTORA* for patients with acute pain, postoperative pain, headache/migraine, or sports injuries**
- ***FENTORA* is not a generic version of Actiq. Therefore, do NOT substitute *FENTORA* for Actiq or other fentanyl-containing products**
- **Follow dosing instructions carefully:**
 - **For unrelieved breakthrough pain (BTP), patients should NOT take more than 2 *FENTORA* tablets per BTP episode**
 - **Patients MUST wait at least 4 hours before treating another BTP episode with *FENTORA***

Please educate your patients as to the importance of following these instructions carefully.

We have revised the patient selection criteria and dosing instructions for *FENTORA*, and will be updating our package insert shortly. Please read the following information about *FENTORA* thoroughly.

Patient Selection

Do not prescribe *FENTORA* to patients who are opioid non-tolerant (i.e., patients who are not taking around-the-clock opioids). Do not prescribe *FENTORA* for patients with acute pain, postoperative pain, headache/migraine, or sports injuries, even if they are suitable for receiving other opioids on an as needed basis (PRN).

***FENTORA* is indicated only for the management of breakthrough pain (BTP) in patients with cancer who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain.** Patients considered opioid tolerant are those who are taking at least 60 mg oral morphine/day, at least 25 mcg transdermal fentanyl/hour, at least 30 mg of oral oxycodone daily, at least 8 mg oral hydromorphone daily or an equianalgesic dose of another opioid for a week or longer.

Dosing Instructions

The following dosing instructions are based on information from the prescribing information for *FENTORA*, with more detail included to clarify questions that have been raised by healthcare professionals:

1. Initial dose

- a. For patients **not** switching from Actiq, the initial titration dose of *FENTORA* is 100 mcg
- b. For patients switching from Actiq, please use the conversion table in the prescribing information for *FENTORA* to select the initial dose. The doses of *FENTORA* in this table are starting doses and not intended to represent equianalgesic doses to Actiq
- c. In cases where the BTP episode is not relieved within 30 minutes of the first dose, patients may take **ONLY 1** additional tablet of the same strength for that episode. If patients have ongoing breakthrough pain after the second dose of *FENTORA*, no further doses of *FENTORA* may be used for that episode of breakthrough pain
- d. Patients **MUST** wait **at least 4 hours** before treating the next breakthrough pain episode with *FENTORA*

2. Dose Titration

- a. **All patients should be titrated to a dose that provides adequate analgesia with minimal side effects** as per the instructions found in the prescribing information. If the initial dose was not able to provide adequate analgesia, the next episode of breakthrough pain may be treated with the next highest dose. If patients have 100 mcg or 200 mcg tablets, the dose may be increased by increasing the number of tablets such that one dose of *FENTORA* may include administration of 2 to 4 tablets of the same dosage strength (100 mcg or 200 mcg)
- b. In cases where the breakthrough pain episode is not relieved within 30 minutes, patients may take **ONLY 1** additional dose of the same strength for that episode
- c. Patients **MUST** wait **at least 4 hours** before treating the next breakthrough pain episode with *FENTORA*
- d. To reduce the risk of overdose during titration, patients should have only one strength *FENTORA* tablets available at any one time

3. Maintenance Dosing

- a. Once titrated to an effective dose, patients should generally use only ONE *FENTORA* tablet per breakthrough pain episode
- b. On occasion, when the breakthrough pain episode is not relieved within 30 minutes, patients may take **ONLY 1** additional tablet of the same strength for that episode
- c. Patients **MUST** wait **at least 4 hours** before treating another breakthrough pain episode with *FENTORA*.
- d. Dosage adjustment of both *FENTORA* and the maintenance (around-the-clock) opioid analgesic may be required in some patients in order to continue to provide adequate relief of pain
 - i. Generally, the *FENTORA* dose should be increased when patients require more than ONE dose to relieve breakthrough pain episode for several consecutive episodes

- ii. If the patient experiences greater than four breakthrough episodes per day, the dose of the maintenance (around-the-clock) opioid used for persistent pain should be re-evaluated

Do not substitute *FENTORA*

Do not substitute *FENTORA* for Actiq or other fentanyl-containing products. The dosage strength of fentanyl in *FENTORA* is not equivalent to the same dosage strength of fentanyl in other fentanyl-containing products. *FENTORA* is a distinct formulation of fentanyl and is NOT a generic version of Actiq. When switching a patient from Actiq to *FENTORA*, physicians must follow instructions found in the prescribing information as Actiq and *FENTORA* are not equivalent on a microgram per microgram basis.

SECURE Program

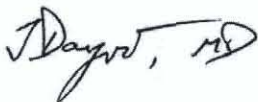
FENTORA has been approved with a comprehensive RiskMAP [SECURE] to minimize risks associated with *FENTORA*, while preserving the product's benefits. The RiskMAP focuses on 3 primary objectives:

1. Ensure that patients and healthcare professionals understand that *FENTORA* should only be used by opioid tolerant patients with cancer
2. Minimize potential for misuse, abuse, and diversion of *FENTORA*
3. Minimize unintended or accidental exposure to *FENTORA*

Thank you for taking the time to read this important safety information on *FENTORA*. Cephalon is committed to providing healthcare professionals with useful information to guide the safe and appropriate use of its products. Before prescribing *FENTORA*, please review the enclosed full prescribing information, including boxed warning. In addition, inform your patients of the availability of a Medication Guide and instruct them to read the Medication Guide with each prescription prior to taking *FENTORA*.

If you have any questions, please contact Cephalon Medical Services at 1-800-896-5855 and we will be glad to assist you. Thank you.

Sincerely,



Jeffrey M. Dayno, M.D.
Vice President
Medical Services

Enclosure: *FENTORA* – Full prescribing information

Important Safety Information for *FENTORA*

PHYSICIANS AND OTHER HEALTHCARE PROVIDERS MUST BECOME FAMILIAR WITH THE IMPORTANT WARNINGS IN THIS LABEL.

***FENTORA* contains fentanyl, an opioid agonist and a Schedule II controlled substance, with an abuse liability similar to other opioid analgesics. *FENTORA* can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing *FENTORA* in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse or diversion. Schedule II opioid substances which include morphine, oxycodone, hydromorphone, oxymorphone, and methadone have the highest potential for abuse and risk of fatal overdose due to respiratory depression.**

***FENTORA* is indicated only for the management of breakthrough pain in patients with cancer who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain.** Patients considered opioid tolerant are those who are taking at least 60 mg of oral morphine/day, at least 25 mcg of transdermal fentanyl/hour, at least 30 mg of oxycodone daily, at least 8 mg of oral hydromorphone daily or an equianalgesic dose of another opioid for a week or longer.

Because life-threatening respiratory depression could occur at any dose in opioid non-tolerant patients, *FENTORA* is **contraindicated** in the management of acute or postoperative pain. **This product is not indicated for use in opioid non-tolerant patients.**

Patients and their caregivers must be instructed that *FENTORA* contains a medicine in an amount which can be fatal to a child. Patients and their caregivers must be instructed to keep all tablets out of the reach of children. (See Information for Patients and Their Caregivers for disposal instructions.)

Due to the higher bioavailability of fentanyl in *FENTORA*, when converting patients from other oral fentanyl products, including oral transmucosal fentanyl citrate (OTFC and Actiq[®]), to *FENTORA*, do not substitute *FENTORA* on a mcg per mcg basis. Adjust doses as appropriate (see DOSAGE AND ADMINISTRATION).

***FENTORA* is intended to be used only in the care of opioid tolerant cancer patients and only by healthcare professionals who are knowledgeable of and skilled in the use of Schedule II opioids to treat cancer pain.**

The concomitant use of *FENTORA* with strong and moderate cytochrome P450 3A4 inhibitors may result in an increase in fentanyl plasma concentrations, and may cause potentially fatal respiratory depression.